REMARKS

Claim status

Claims 1-137 are pending in the present application. Claims 128-137 are withdrawn from consideration following Applicants' election of an invention upon which claims 1-127 read. Claims 1-127 stand rejected on arguments laid out in a non-final Office Action mailed on April 1, 2000.

Claim amendments

Claims 1, 16-17, 43, 47-48, 84, 92-93, 110-111, and 131 are amended by the present amendment. Claims 1, 43, and 84 are amended to recite that the fetal DNA is obtained from amniotic fluid that is cell-free. Claim 1 is also amended to recite analyzing fetal DNA by *genomic* hybridization. Support for these amendments can be found in the specification, for example, on page 5 (lines 23-24), page 6 (lines 16-21), and page 14 (lines 27-29). Claims 16-17, 47-48, 92-93, 110-111, and 131 are amended to properly recite trademarked names in capital letters. Claim 95 is also amended to correct the informality of missing a period at the end. Claims 18, 49-50, 94-95, and 112-113 are canceled without prejudice by the present amendment. No new claims are added.

Applicants submit that no new matter is introduced by the present amendment.

Therefore, after entrance of the present amendment, claims 1-17, 19-48, 51-93, 96-137 are pending and presented for examination.

Amendments to the specification

The specification has been amended in order to capitalize trademarked names CY™-3, CY™-5, TEXAS RED™, SPECTRUM RED™, SPECTRUM GREEN™, and GENOSENSOR™. Applicants submit that no new matter is introduced by the present amendment.

Claim objections

The Office Action objected to claim 95 because of the informality of missing a period. Claim 95 has been amended to correct the informality.

The Office Action has also noted that trademarks should be capitalized wherever they appear. Claims 18, 49-50, 94-95, and 112-113 are canceled. Claims 16-17, 47-48, 92-93, 110-111, and 131 and relevant parts of the specification have been amended accordingly.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 16-18, 47-50, 92-95, and 110-113 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for reciting trademarks. In particular, the Examiner states that "A trademark or trade name is used to identify a source of goods, not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a fluorescent label and, accordingly, the identification/description is indefinite" (page 3 of the Office Action).

Without acquiescing to the Examiner's comments regarding the use of trademarks, Applicants have canceled or amended claims that refer to the trademarks SPECTRUM RED™ and SPECTRUM GREEN™ such that they are no longer recited in the claims.

Applicants respectfully submit that the use of trademark CY™ in the names "CY™-3" and "CY™-5" does not render the claims indefinite. CY™ is a registered trademark of Amersham Biosciences Limited, but CY™-3 and CY™-5 refer to specific cyanine dyes having particular chemical structures. Both the dyes themselves and their physical characteristics (including their chemical structures) are known to and available to those of ordinary skill in the art, and were available at the time of filing of the present application. The Examiner's attention is drawn to the attached product specification brochures (submitted as **Exhibit A**) from Amersham Biosciences dated in the year 2000. These brochures describe products containing CY™-3 and CY™-5 dyes and show the chemical structures of each fluorescent dye. Furthermore, the chemical names of CY™-3 and CY™-5 are provided in the specification, for example, on page 29, lines 18-19 as 3- and 5-N,N'-diethyltetramethylindocarbocyanine respectively.

Applicants submit that given the knowledge in the art at the time of filing and the information provided in the present specification, one of ordinary skill in the art would have no doubt as to which fluorescent dyes are meant by "CY™-3" and "CY™-5".

For all these reasons, Applicants respectfully submit that the claims, as amended, satisfy the requirements of 35 U.S.C. § 112, second paragraph. Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-3, 5, 6, 12-15, 19, 22, 25-26, 28-31, 34, 35, and 38 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Bianchi *et al.*[1] (hereinafter 'Bianchi').

Claim 1 as amended recites "analyzing the amniotic fluid fetal DNA by *genomic* hybridization to obtain fetal genomic information." (emphases added). Bianchi does not teach using genomic

[1] *Clinical Chemistry*. Oct. 2001. **47**:1867-1869; cited in the IDS filed May 10, 2007

hybridization at all. Because Bianchi fails to teach each and every claim limitation of claim 1 and its dependents, Bianchi cannot anticipate claims 1-3, 5, 6, 12-15, 19, 22, 25-26, 28-31, 34, 35, and 38. Applicant respectfully requests that this rejection be removed.

Claims 1, 2, 4, 14-17, 19, 21-26, 28-31, 33, 34, 35, and 38 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Lapierre *et al.*[2] (hereinafter "Lapierre").

Claim 1 as amended recites "providing a sample of fetal DNA *from cell-free amniotic fluid*." (emphases added). Lapierre does not teach using fetal DNA from cell-free amniotic fluid. Lapierre clearly refers to using DNA from cells, as they refer to using techniques on uncultured amniocytes (see Abstract) and perform analyses on chromosomes prepared from cells (see column one on page 124, which describe experimental procedures on amniotic fluid containing cells). Because Lapierre fails to teach each and every limitation of claim 1 and its dependents, Lapierre cannot anticipate claims 1, 2, 4, 14-17, 19, 21-26, 28-31, 33, 34, 35, and 38.

Applicants respectfully request that this rejection be removed.

Claim rejections under 35 U.S.C. § 103(a)

1. Claims 8 and 9 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bianchi in view of Pinkel[3]. Applicants respectfully traverse this rejection on the grounds that it would not have been obvious to combine Bianchi and Pinkel to arrive at the claimed invention. The present claims recite using fetal DNA from cell-free amniotic fluid.

In referencing analysis of amniotic fluid for prenatal diagnosis, Pinkel clearly refers to analysis of samples containing cells:

> "Small numbers of cells obtained from aspiration biopsy or cells in bodily fluids… can also be analyzed. For prenatal diagnosis, appropriate samples will include amniotic fluid and the like." (column 9, lines 46-49)

There is no teaching or suggestion in Pinkel that it would be desirable to use cell-free amniotic fluid.

[2] *Prenatal Diagnosis*. 2002. **20:**123-131; cited in the IDS filed May 7, 2007
[3] U.S. Pat. No. 6,210,878

Furthermore, it would not have been obvious to combine Bianchi with any reference in the context of prenatal diagnostics. Bianchi does not concern itself with prenatal diagnostic applications of using DNA from cell-free amniotic fluid, and is instead interested in the biological origins of such DNA. Bianchi's focus is evident, for example, in their concluding statement, which does not discuss how their findings may be applied to prenatal diagnostic applications. Instead, their concluding statement focuses on the biological origins of such DNA:

> "Although the present study adds another piece to the puzzle, our findings do not solve the mystery of how the pregnant woman clears the fetal DNA from her circulation. In fact, it raises more questions, such as how the fetus eliminates the DNA from its amniotic cavity. Does the fee DNA cross the placenta, or is it swallowed and degraded in the fetal intestines? Future studies will attempt to identify the specific tissue of origin of the fetal DNA in amniotic fluid and track its metabolism and/or transfer into the circulation of the pregnant woman" (column 1, page 1869)

For these reasons, Bianchi in combination with Pinkel cannot render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

2. Claims 9 and 10 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bianchi in view of Fan[4].

Fan does not teach or suggest any applications of their work in relation to prenatal diagnosis, let alone diagnosis of DNA from cell-free amniotic fluid. As discussed above, Bianchi is not concerned with prenatal diagnostic applications. Therefore, Bianchi in combination with Fan cannot render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

3. Claims 20, 36, and 37 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Bianchi in view of Bianchi (U.S. Patent No. 5,714,325; hereinafter "the '325 patent").

As discussed above, Bianchi is not concerned with prenatal diagnostic applications and it would not be obvious to combine Bianchi with other references in the context of prenatal diagnosis. Therefore, Bianchi in combination with the '325 patent cannot render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

[4] *Genome Research.* 2000. **10:**853-860

4. Claims 7, 11, 29, 32, 39-48, 51-54, 56, 59-67, 69-76, 79-88, 90-93, 96, 97, 99, 102-111, 114, 115, 117, 118, 120, and 124-127 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Veltman[5].

The claims as amended recite using fetal DNA from cell-free amniotic fluid. Veltman describes the results therein as possibly having a "profound impact on the diagnosis and genetic counseling of patients with mental retardation" (page 1275, second-to-last paragraph of column 1) and does not discuss or suggest analysis of amniotic fluid at all. Neither Lapierre nor Veltman teach or suggest using fetal DNA from *cell-free* amniotic fluid, as recited by the present claims. For these reasons, Lapierre in combination with Veltman cannot render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

5. Claim 18 is rejected under 103(a) as being allegedly unpatentable over Lapierre in view of Muller[6]. Claim 18 has been canceled by the present amendment, thereby rendering this rejection moot.

6. Claims 49, 50, 94, 95, 112, and 113 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Lapierre in view of Veltman, and further in view of Muller. Claims 49, 50, 94, 95, 112, and 113 have been canceled by the present amendment, thereby rendering this rejection moot.

7. Claim 27 stands rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Sammons[7].

As discussed above, Lapierre does not teach or suggest using fetal DNA from *cell-free* amniotic fluid, as recited by the present claims. Sammons does not cure this deficiency, as Sammons does not teach or suggest using DNA from cell-free amniotic fluid. In fact, Sammons is concerned with methods of separating and/or enriching rare cell populations for analysis of such cells. (See, *e.g.*, Abstract and column 1, lines 15-23.) For these reasons, Lapierre in combination with Sammons cannot render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

8. Claim 68 stands rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Veltman and Sammons.

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[5] *American Journal of Human Genetics*. 2002. **70**:1269-1276; cited in the IDS filed September 11, 2007
[6] U.S. Pat. No. 6,306,589
[7] U.S. Pat. No.

The claims as amended recite using fetal DNA from cell-free amniotic fluid. As discussed above, none of these references (Lapierre, Veltman, and Sammons) teach or suggest using fetal DNA from cell-free amniotic fluid. No combination of Lapierre, Veltman, and Sammons can render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

9. Claims 55, 57, 98, 100, 116, 119, and 121 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Veltman and further in view of Bianchi. The claims as amended recite using fetal DNA from cell-free amniotic fluid. As discussed above, Veltman does not discuss or suggest analysis of amniotic fluid at all, and Lapierre lacks any teaching or suggestion with respect to analysis of fetal DNA from cell-free amniotic fluid. Also as discussed above, Bianchi is not concerned with prenatal diagnostic applications and it would not be obvious to combine Bianchi with other references in the context of prenatal diagnosis. Therefore, no combination of Bianchi, Lapierre, and Veltman can render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

10. Claims 58, 101, 122, and 123 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Veltman, Bianchi, and further in view of Shah[8].

The claims as amended recite using fetal DNA from cell-free amniotic fluid. As mentioned above, no combination of Lapierre, Veltman, and Bianchi renders obvious using fetal DNA from cell-free amniotic fluid for prenatal diagnostic applications as recited in the present claims. Shah does not cure this deficiency, as Shah fails to teach or suggest using the computer systems therein for analysis of fetal DNA from amniotic fluid, let alone from cell-free amniotic fluid.

11. Claims 77 and 78 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Veltman and further in view of the '325 patent.

The claims as amended recite using fetal DNA from cell-free amniotic fluid. As discussed above, Lapierre in combination with Veltman fails to render obvious the claimed invention. The '325 patent fails to cure this deficiency. Therefore, no combination of Lapierre, Veltman, and the '325 can render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

12. Claim 89 stands rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Lapierre in view of Veltman and further in view of Pinkel.

[8] U.S. Pat. No. 6,916,621

The claims as amended recite using fetal DNA from cell-free amniotic fluid. None of LaPierre, Veltman, and Pinkel teach or suggest that it would be desirable to use fetal DNA from cell-free amniotic fluid. Thus, no combination of LaPierre, Veltman, and Pinkel can render obvious the claimed invention. Applicants respectfully request withdrawal of this rejection.

In view of the above remarks, Applicants respectfully request that the Examiner reconsider and withdraw the outstanding rejections. Favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited. It is believed that all fees due with this response are being submitted herewith. If any additional fees necessary to keep the present case pending and/or to protect the filing date are due, or any overpayment has been made, authorization is hereby given to charge or credit Deposit Account No. 03-1721 for any deficiencies or overages in connection with this response. No authorization is permitted to charge "optional" fees, *e.g.*, excess claims fees. In any event wherein the USPTO believes that additional fees are due, a Notice to that effect is respectfully requested.

Respectfully submitted,

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